UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY
CAMDEN VICINAGE

IN RE: VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION **This Document Relates to All Actions**	MDL No. 2875 Honorable Robert B. Kugler, District Court Judge Oral Argument Requested

MEMORANDUM OF LAW IN SUPPORT OF DEFENDANTS' JOINT MOTION TO EXCLUDE THE OPINIONS OF DIPAK PANIGRAHY, M.D.

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Defendants Executive Committee, on behalf of all Defendants in this litigation, respectfully submit this Memorandum of Law in support of Defendants' Joint Motion to Exclude the Opinions of Dipak Panigrahy, M.D., pursuant to Federal Rules of Evidence 702, 403, and 104.

INTRODUCTION

Plaintiffs have disclosed Dr. Dipak Panigrahy, an unlicensed medical doctor, to offer general causation opinions establishing a purported link between the exposure to N-nitrosodimethylamine ("NDMA") and N-nitrosodiethylamine ("NDEA") in valsartan-containing drugs ("VCDs") and the development of various cancers in humans. Dr. Panigrahy opines in general terms that NDMA can either "cause" or "increase the risk" of liver, bladder, blood, gastric, intestinal, pancreatic, esophageal, prostate, lung, and kidney cancer in humans. (*See generally* Rule 26 Expert Report of Dipak Panigrahy, MD ("Panigrahy Rep."), attached as Ex. A). Dr. Panigrahy's opinions cannot assist the Court or a jury on the essential general causation question before the Court: whether the NDMA or NDEA levels to which valsartan patients could reasonably have been exposed increases the risk of any of the above cancers, let alone all of them. His general causation opinions are and unreliable, and he is unqualified to give them.

First, Dr. Panigrahy bases his general causation opinions on unreliable methodologies. Among his methodological deficiencies, he endorses the unscientific

"single molecule theory" that numerous courts have rejected and excluded as scientifically meritless; he uses the FDA's acceptable daily intake limit as an improper proxy for general causation; he ignores the role of DNA repair entirely; he relies on an inapposite inhalation exposure study; and he improperly assumes without any scientific basis that VCDs contain sufficient quantities of NDMA to escape the liver and reach other "downstream organs."

Second, Dr. Panigrahy grounds his opinions on unreliable data. He cherry-picks the highest identified levels of NDMA and NDEA as the premise for each of his general causation opinions. He further employs inflated calculations inconsistent with real-life exposure levels.

Third, Dr. Panigrahy is not qualified to offer his opinions as to whether NDMA or NDEA cause cancer or increase the risk of developing cancer in humans.

SPECIFIC OPINIONS TO BE EXCLUDED[1]

Defendants move to exclude the opinions offered by Dr. Panigrahy in their entirety, including the following:

[1]Defendants reserve the right to move to exclude or limit this expert witness's opinions on grounds other than those set forth herein if those grounds become available subsequent to the filing of this Motion by virtue of the additional deposition time with Dr. Panigrahy pursuant to the Court's ruling on September 29, 2021 (*see* Special Master Order 45, [Dkt. 1590]), any additional discovery that may take place in this case, or supplementation of this expert witness's disclosure or Report.

- NDMA and NDEA cause the following human cancers: colorectal/intestinal, esophageal/pharyngeal, gastric, kidney, liver, lung, pancreatic, prostate, bladder and blood.
- Based on valsartan dosing and levels of NDMA and NDEA reported in certain batches of valsartan, and the time frame over which those impurities existed, it is medically and scientifically plausible that a number of users of valsartan have already or will develop clinical cancer.
- Exposure to NDMA and/or NDEA at the levels measured in valsartan can initiate and/or promote cancer growth.
- Continued exposure to NDMA and/or NDEA can cause an existing cancer to grow, metastasize and otherwise interfere with cancer therapy.

Alternatively, Defendants request that the Court limit Dr. Panigrahy's opinions to those opinions, if any, on which he shows himself to be qualified and for which his methodology is reliable.

FACTUAL AND PROCEDURAL BACKGROUND

Defendants hereby adopt and expressly incorporate by reference the "Factual and Procedural Background" set forth in the Memorandum of Law in Support of Defendants' Joint Motion to Exclude the Opinions of Stephen Hecht, Ph.D.

LEGAL STANDARDS

In addition to the legal standards set forth herein, Defendants incorporate by reference the section entitled "Legal Standards" set forth in the Memorandum of Law in Support of Defendants' Joint Motion to Exclude the Opinions of Stephen Hecht, Ph.D.

Under Federal Rule of Evidence 702, this Court performs a "gatekeeping function" to ensure that all expert testimony is both relevant and reliable. *See In re Paulsboro Derailment Cases*, 746 Fed. Appx. 94, 98 (3d Cir. 2018) (Vanaskie, J.) (citing *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 589 (1993)); It is Plaintiffs' burden alone to show Dr. Panigrahy's testimony is admissible. *See Warren Distributing Co. v. Inbev USA L.L.C*, 2010 WL 2179167, at *3 (D.N.J. May 26, 2010) (Kugler, J.) (citing *Kannankeril v. Terminix Int'l, Inc.*, 128 F.3d 802, 806 (3d Cir. 1997)).

"Rule 702 embodies a trilogy of restrictions on expert testimony: ***qualification***, ***reliability***, and ***fit***." *Ruggiero v. Yamaha Motor Corp., U.S.A.*, 778 F. App'x 88, 93 (3d Cir. 2019) (emphasis added) (quoting *Schneider ex rel. Estate of Schneider v. Fried*, 320 F.3d 396, 404 (3d Cir. 2003)). First, the Court must consider whether the expert is qualified "to render an opinion" based on his or her "specialized expertise." *In re Hum. Tissue Prods. Liability Litig.*, 582 F. Supp. 2d 644, 655 (D.N.J. 2008) (quoting *Pineda*, 520 F.3d at 244). Though qualification is

interpreted liberally, the Third Circuit recognizes an expert who "may be generally qualified" may nevertheless "lack qualifications to testify outside his area of expertise." *Calhoun v. Yamaha Motor Corp., U.S.A.*, 350 F.3d 316, 322 (3d Cir. 2003). Second, the Court must evaluate the reliability of the expert's methodology. For a methodology to be reliable, the expert's opinions must be based on methods and procedures of science rather than on subjective belief or unsupported speculation. The expert must have "good grounds" for his or her belief. *See In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 732 (3d Cir. 1994) (quoting *Daubert*, 509 U.S. 579 at 590). Third, the Court must consider whether the expert's testimony will be helpful to the trier of fact. *See* Fed. R. Evid. 702(a). "The issue of fit 'is one of relevance and expert evidence which does not relate to an issue in the case is not helpful.' . . . The standard for fitness is 'not that high' but is 'higher than bare relevance.'" *In re Hum. Tissue Prod. Liab. Litig.*, 582 F. Supp. 2d at 657 (quoting *In re TMI Litig.*, 193 F.3d 613, 670 (3d Cir. 1999); *In re Paoli*, 35 F.3d at 745). An opinion fits and helps the trier of fact when there is a connection between the scientific research or test result presented and the particular disputed factual issues in the case. *Warren Distributing Co.*, 2010 WL 2179167, at *4.

ARGUMENT

I. DR. PANIGRAHY'S OPINIONS ARE UNRELIABLE BECAUSE THEY REST ON UNRELIABLE METHODOLOGIES.

A. Dr. Panigrahy's Opinion That NDMA and NDEA Can Cause Human Cancers Relies on an Unreliable "Single Molecule" Theory and Should Be Excluded.

Dr. Panigrahy's opinions are methodologically unreliable. Indeed, they rest on a methodology courts have repeatedly considered and rejected as scientifically meritless. Proving general causation in toxic tort cases requires relevant and ***reliable*** expert testimony that a particular chemical is harmful to humans. *See Zellars v. NexTech Northeast, LLC*, 895 F. Supp. 2d 734, 739 (E.D. Va. 2012) (citing *McCallum ex rel. McCallum v. United States*, 2005 WL 1048735, at *10 (E.D. Va. May 4, 2005)). "In order to carry the burden of proving a plaintiff's injury was caused by exposure to a specified substance, the plaintiff must demonstrate the levels of exposure that are hazardous to human beings generally as well as the plaintiff's actual level of exposure." *Id.* Stated differently, the plaintiff must show the level of exposure required to cause the plaintiff's condition. *See id.* Dr. Panigrahy fails do so and instead relies on an untenable (and oft excluded) "each and every exposure" theory, which he calls "single exposure." (Panigrahy Dep. 309:8-13, transcript attached as Ex. B); *see also e.g.* Memorandum of Law in Support of Defendants' Joint Motion to Exclude the Opinions of Stephen Hecht, Ph.D. ("Motion to Exclude Hecht"), at Section II(B)(1) (explaining that "Dose is the single most important

factor to consider in evaluating whether an alleged exposure caused a specific adverse effect.").

Dr. Panigrahy's basis for his opinion that NDMA and NDEA cause liver, bladder, blood, gastric, intestinal, pancreatic, esophageal, prostate, lung, and kidney cancer in humans rests on the unsubstantiated assertion that ***any*** exposure to NDMA can cause cancer. (*Id.* at 185:5-8). However, each cancer is unique and has different etiologies. Dr. Panigrahy simply conflates cancer generally with the specific cancers at issue without adequately establishing a causal connection to NDMA or NDEA. Moreover, as set forth below, Dr. Panigrahy fails to analyze whether NDMA and NDEA could escape first-pass metabolism to even reach downstream organs (i.e., organs that receive blood flow after liver metabolism). He asserts: "Even a molecule could cause cancer." (*Id.*). He then doubles down on this claim: "We know from multiple years of experience with genotoxic carcinogens there's no safe dose, because even one molecule can induce DNA damage." (*Id.* at 357:5-8). Dr. Panigrahy thus believes, incorrectly, that because exposure to one molecule of NDMA can allegedly induce DNA damage, exposure to one molecule is capable of causing cancer. That conclusion defies accepted scientific understanding and basic logic, ignores the well-established DNA repair defenses (discussed *infra*), and is not grounded in any medical literature or other reliable source. It is pure *ipse dixit.*

Dr. Panigrahy offers no scientific basis for his view that "one molecule" is a cancer-inducing exposure. He makes no attempt to identify a scientifically reliable estimate of the threshold level of NDMA or NDEA that can induce DNA damage sufficient to cause cancer, much less explain why the threshold level is one molecule. He fails to establish—or even consider—what actual level of NDMA or NDEA exposure was reasonably likely for a valsartan patient, or why that exposure level could be sufficient to play a causative role in the development of cancer or increase the risk of cancer in these patients. Without grounding his "one molecule" theory in science, his opinions are inherently unreliable and should be excluded.

Courts across the country have recognized the dose-dependent nature of carcinogenesis. Section II(B)(1) (explaining that "Dose is the single most important factor to consider in evaluating whether an alleged exposure caused a specific adverse effect."). "'Ruling in' exposure to a particular substance as a possible cause of a patient's medical condition requires (1) a reliable determination of the level of exposure necessary to cause the condition and (2) a reliable determination that the patient was exposed to the substance at that level." *Zellars*, 895 F. Supp. 2d at 742.

Accordingly, courts have repeatedly rejected the so-called "each and every exposure" theory as unreliable under Rule 702 and *Daubert*. *See, e.g.*, *Krik v. Exxon Mobil Corp.*, 870 F.3d 669, 674-675 (7th Cir. 2017) (noting that the any exposure theory ignores fundamental principles of toxicology as illnesses like cancer are dose

dependent); *Rockman v. Union Carbide Corp.*, 266 F. Supp. 3d 839, 849 (D. Md. 2017) (noting that prevailing authority applying *Daubert* has rejected the "each and every exposure" causation theory as it is not the product of reliable principles and methods nor does it enjoy general acceptance within the relevant scientific community); *Yates v. Ford Motor Co.*, 113 F. Supp. 3d 841, 846 (E.D.N.C. 2015) (citing numerous decisions[2] rejecting the each and every exposure theory as lacking sufficient support in facts or data and decisions finding that the theory cannot be tested, has not been published in peer-reviewed works, and has no known error rate); *see also* Motion to Exclude Hecht, at Section II(B)(3) (explaining that courts do not use the "no safe level" theory because it is unreliable).

Dr. Panigrahy's "one molecule" theory is simply the "each and every exposure" theory under a different name. His insistence that "one molecule" of NDMA is enough to damage DNA, and therefore to cause cancer, is no different in its premise or conclusion from the unscientific claim that "each and every" exposure to an alleged carcinogen can cause cancer without regard to dose, timing, or response. A more rigorous analysis is required to move from mere armchair musings

[2] *Comardelle v. Pa. Gen. Ins. Co.*, 76 F. Supp. 3d 628 (E.D. La. 2015); *Krik v. Crane Co.*, 71 F. Supp. 3d 784 (N.D. Il 2014); *Anderson v. Ford Motor Co.*, 950 F. Supp. 2d 1217, (D. Utah 2013); *Sclafani v. Air & Liquid Sys. Corp.*, 2013 WL 2477077, at *5 (C.D. Cal. May 9, 2013); *Henricksen v. ConocoPhillips Co.*, 605 F. Supp. 2d 1142, 1166 (E.D. Wash. 2009).

into a scientifically grounded, data-supported causation conclusion. Dr. Panigrahy's "one molecule" theory is a flight of fancy, not a scientific opinion. *See* Motion to Exclude Hecht, at Section II(B)(3) (explaining that "more than thirty other federal courts and state courts have held that this cumulative/'any exposure' theory is not reliable").

The exposure levels claimed by Plaintiffs in this litigation were readily available[3] for Dr. Panigrahy to evaluate and to test whether the alleged exposures, as a general proposition, were enough under established medical and scientific research to establish a causal role in or an increased risk of the development of cancer. Dr. Panigrahy simply elected not to consider the available data. He cannot identify any Plaintiff's level of exposure to NDMA and/or NDEA; he simply assumes every patient was consistently exposed to the highest levels measured in a single valsartan pill. (Panigrahy Dep. 495:16-496:7).

More than that, Dr. Panigrahy's analysis eschews human studies evaluating real-life levels of human exposure to NDMA and/or NDEA in VCDs in favor of studies of NDMA and NDEA exposure in experimental animals with doses hundreds of times greater than the levels measured in the VCDs at issue here. (Panigrahy Dep. 189:21-190:8). Dr. Panigrahy also ignores the endogenous level of NDMA produced

[3] *See* Discussion in Section II(A), *infra.*

in humans every day, even as he admits there is an endogenous process for forming NDMA occurring independent of dietary NDMA. (*Id*. 237:5-238:15). He failed to perform any independent calculations accounting for endogenous NDMA. (*Id.* 523:4-14).

The data and information Dr. Panigrahy failed to consider underscore why he must rely on his unscientific "one molecule" theory. "A plaintiff must show that the exposure to each defendant's product was a substantial factor in causing or exacerbating the disease." *Steele v. Aramark Corp.*, 535 Fed. App'x 137, 140 (3d. Cir. 2013). Yet Plaintiffs wish to reframe the general causation inquiry to avoid the critical (and legally necessary) issues of substantial factor, dose, response, and timing, and simply argue that any exposure at all is assumed to be causative. Dr. Panigrahy's "one molecule" theory fails to consider any dose threshold, fails to account for the role of DNA repair, does not distinguish between environmental and dietary NDMA exposure versus exposure through VCDs, and ignores endogenous levels of NDMA.

Moreover, Dr. Panigrahy's theory is notably at odds with FDA's own views, as even the agency's highly conservative daily acceptable intake level of 96 nanograms equates to approximately 725 ***trillion*** molecules of exposure. (Chodosh Dep. 350:22-351:20, excerpts attached as Ex. C). Dr. Panigrahy was unable to reconcile his one molecule theory with the FDA's determination that up to 96

nanograms per day of NDMA and 26.5 nanograms per day in ARBs is safe. (Panigrahy Dep. 357:21-358:11). Dr. Panigrahy's one molecule theory cannot be reconciled with his own testimony that a level of NDMA orally taken would be successfully metabolized with first-pass metabolism as well. If a level of orally taken NDMA would be successfully metabolized with first-pass metabolism, this safe level must already exceed one molecule as defined and used by Dr. Panigrahy. (*See* Panigrahy Dep. at 438:13-21) ("Q. Doctor, the exposure to the levels of NDMA detected in the valsartan tablets because of oral ingestion, would first go -- first be metabolized by the liver, correct? A. Correct. [ ]"; (Panigrahy Dep. at 441:17-20) ("Q. Doctor, there is a level of NDMA that would be successfully metabolized with first-pass metabolism; isn't that correct? A. Correct.").

Even Plaintiffs' epidemiology expert, Dr. Mahyar Etminan, testified that there was likely no increased risk with taking valsartan for thirty or even ninety days. (Etminan Dep., Vol II, 62:5-22, excerpts attached as Ex. D). A general causation opinion must be grounded in something more than Dr. Panigrahy's speculative ponderings. His opinions are ungrounded and should be excluded.

B. Dr. Panigrahy's Opinions Use the FDA's Daily Acceptable Intake Level as an Improper Proxy for General Causation.

Dr. Panigrahy's conclusion that exposure to NDMA results in an increased risk of cancer is further based on the finding that the level of NDMA in some VCDs exceeded the FDA's acceptable intake limit. Dr. Panigrahy undertook no research

and performed no calculations to actually determine whether the level of microgram exposure in the VCDs increases the risk of cancer in the patients exposed. Instead, Dr. Panigrahy equates exposure above the FDA's daily acceptable intake level with proof of general causation. But that view lacks a reliable scientific basis and cannot establish general causation. *See* Motion to Exclude Hecht, at Section II(B)(4) (discussing the law establishing that public health guidelines are not the level at which harmful effects occur and cannot be used to establish general causation).

It is well-established that public health guidelines, which include the FDA's acceptable daily intake limits for NDMA and NDEA, cannot be used as a proxy to establish tort liability in federal court. *See McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1249-50 (11th Cir. 2015) (excluding testimony of proffered toxicology expert whose opinion was "more adjusted to agency-risk analysis than courtroom-causation analysis"); *Rider v. Sandoz Pharms. Corp.*, 295 F.3d 1194, 1201 (11th Cir. 2002) (cautioning, "[a] regulatory agency such as the FDA may choose to err on the side of caution. Courts, however, are required under the *Daubert* trilogy to engage in objective review of evidence to determine whether it has sufficient scientific basis to be considered reliable."); *Mancuso v. Consol. Edison Co. of New York*, 967 F. Supp. 1437, 1448–49 (S.D.N.Y. 1997) ("Failure to meet regulatory standards is simply not sufficient to establish general causation"). Indeed, there is a crucial distinction to be made between the Court's gatekeeping function under Rule 702,

and FDA's public health role, which is "to reduce public exposure to harmful substances." *Glastetter v. Novartis Pharms. Corp.*, 252 F.3d 986, 991 (8th Cir. 2001) (citations omitted). Indeed, "***[t]he FDA will remove drugs from the marketplace upon a lesser showing of harm to the public than the preponderance-of-the-evidence or more-likely-than-not standards used to assess tort liability***." *Id.* This is because the FDA must apply "worst-case" assumptions, particularly when its allowable exposure limits must apply broadly to large, diverse populations, ranging from young to old, and from the healthy to the terminally ill. *McClain*, 401 F.3d at 1249. Thus, "risk assessors may pay heed to any evidence that points to a need for caution, rather than assess the likelihood that a causal relationship in a specific case is more likely than not." *Id.* (citing Margaret A. Berger, *The Supreme Court's Trilogy on the Admissibility of Expert Testimony,* REFERENCE MANUAL ON SCIENTIFIC EVIDENCE, 33 (Federal Judicial Center, 2d. ed.2000)). Accordingly, regulators like FDA "generally overestimate potential toxicity levels for nearly all individuals." *Id.*

In contrast, in order to sustain their burden at trial, Plaintiffs must demonstrate causation, not mere risk. Dr. Panigrahy erroneously bases his core opinion that affected VCDs can cause cancer in humans on the fact that some of the medications

tested exceeded FDA's allowable daily intake limits.[4] Dr. Panigrahy ignores the fact that FDA's allowable daily intake limits are extremely conservative estimates meant to curtail an infinitesimal risk to the population at large. These limits are not intended to establish—and cannot establish—a causal relationship between consuming affected VCDs and developing cancer. In essence, Dr. Panigrahy is improperly assessing risk, not causation. It is not sufficient for Dr. Panigrahy to merely identify a risk factor. This is the purview of health authorities like FDA; it is not the proper role of a testifying expert with respect to general causation and conclusions that falsely equate a risk factor with general causation are inherently unreliable.

C. Dr. Panigrahy Ignores the Role of DNA Repair, which Directly Affects any Risk Assessment.

Dr. Panigrahy's conclusions are also unreliable because they fail to consider and account for the role of DNA repair mechanisms, which have been shown to effectively repair the specific mutation caused by NDMA. Dr. Panigrahy admits these mechanisms exist and can result in the error-free repair of the same adducts he alleges would lead to cancer. (Panigrahy Dep. 275:7-13). Yet his analysis ignores the DNA repair mechanisms altogether as an inconvenient obstacle to his predetermined result. That is advocacy, not science.

[4]Dr. Panigrahy admits that some defendants' levels of NDMA were in fact lower than the FDA's acceptable daily limit. (*See* Panigrahy Dep. 501:7-24).

As discussed above, Dr. Panigrahy's opinion that NDMA causes cancer is based on his bald assertion that any exposure to NDMA can induce DNA damage and ergo cause cancer. (*Id.* at 357:5-8). Even accepting that unscientific and unsubstantiated premise for the sake of argument, deriving the conclusion that potential DNA damage causes cancer without accounting for the role of DNA repair is inherently unreliable, and risks confusing and misleading the jury. Dr. Panigrahy admits that DNA repair mechanisms exist for the mutation caused by NDMA and can result in error-free repair of mutation-causing adducts. (*Id.* at 275:7-13). He did not account for those mechanisms in offering his opinions here.

Dr. Panigrahy's sole justification for failing to account for the role of DNA repair is that he believes that NDMA can impair the DNA repair enzyme. (*Id.* at 275:7-20). That is again nothing more than his *ipse dixit*; he does not cite any reliable study or scientific data to back up his belief, because there is none. Dr. Panigrahy is unable to identify any peer-reviewed article concluding that NDMA interferes with the DNA repair process in humans. (*Id*. at 280:6-281:23). He is only able to point to inapposite animal studies evaluating the effects of NDMA in animals at much higher doses than what were present in any VCDs. (*Id*. at 189:21-190:8).

Dr. Panigrahy likewise has no basis for his view that some level of NDMA exposure could overwhelm the body's DNA repair mechanisms, much less to claim that the real-world levels of exposure at issue here could do so. And he further

undercuts his methodology by acknowledging that the DNA repair capacity in humans is far greater than the DNA repair capacity in animals. (*Id.* at 190:23-191:8). Again, his failure to account for levels and duration of NDMA exposure a patient could reasonably have been exposed to here is a result of his steadfast and misplaced reliance on his "single molecule" theory, and the inherent unreliability of his assumptions permeates each of his opinions in this case. The Court should exclude his opinions as unreliable and without scientific basis.

D. Dr. Panigrahy's Heavy Reliance on the Hidajat Study Is Misplaced.

The primary, and in some instances sole basis cited by Dr. Panigrahy in support of his opinion that NDMA causes certain types of cancer is a single occupational study—Hidajat et al.—that examined British rubber industry workers who inhaled large quantities of NDMA and other carcinogenic substances over a period of decades, and found statistically significant associations between that exposure and several cancers. (Panigrahy Dep. 483:9-12; (Ex. E, Hidajat, et al.). Dr. Panigrahy's heavy reliance on Hidajat is misplaced because he largely ignores Hidajat's significant limitations, which include (i) the exponentially higher levels of NDMA exposure in Hidajat compared to those at issue here; (ii) the different mode of exposure—inhalation versus oral ingestion; and (iii) the study's failure to analyze important confounding factors. As a result of these limitations, the Hidajat study

does nothing to establish a causal association between NDMA at the levels found in the affected VCDs and cancer.

Dr. Panigrahy admitted that the level of NDMA exposure in Hidajat was many orders of magnitude higher than the potential NDMA exposure at issue here. Specifically, based on Dr. Panigrahy's own calculations, the cumulative annual NDMA exposures of the rubber works in Hidajat, by quartile, were as follows:

- Quartile I: baseline (study made no attempt to quantify);
- Quartile II: 7,488,000 nanograms;
- Quartile III: 14,304,000 nanograms; and
- Quartile IV: 23,208,000 nanograms.

(*Id.* at 486:7-488:21; Panigrahy Rep. at 87). Notably, this annual exposure occurred over a period of forty-nine (49) years. (Panigrahy Dep. 499:21-500:10). Not surprisingly, Dr. Panigrahy could not identify a single Plaintiff in this litigation who could have been exposed annually to enough NDMA from a VCD to reach Quartile II, let alone the higher quartiles of NDMA exposure identified in Hidajat. (*Id.* at 497:20-499:8). This alone renders Hidajat irrelevant to the causation analysis in this litigation. (*Id.* at 497:20-499:8).

Moreover, Dr. Panigrahy acknowledged that these workers were also exposed to other nitrosamines in addition to NDMA. (*Id.* at 489:14-21). Again, using Dr. Panigrahy's own calculations, he would be able to calculate a "total nitrosamine

score" that is even higher than the NDMA exposures in Quartiles II-IV. (*Id.* at 489:22-493:5). For example, the total annual nitrosamine score for Quartile II, would be approximately 24,000,000 to 51,000,000 nanograms. (*Id.* at 499:10-17). This astronomical figure is completely incongruent with the potential levels of nitrosamines exposure at issue in this litigation.

The second key limitation of Hidajat is the different mode of NDMA exposure. Specifically, the rubber workers in Hidajat were exposed to NDMA through inhalation of particles in the air, whereas the purported exposure here is through oral ingestion of VCDs. This is a key distinction because, as Dr. Panigrahy admits and as discussed more fully *infra*, orally ingested NDMA will be metabolized first in the liver, and will never reach other downstream organs (*Id.* at 440:24-441:4; 441:17-23). In contrast, NDMA that is inhaled results in systemic exposure, which is necessarily metabolized differently (*Id.* at 433:24-434:23). As a result, these modes of exposure are inapposite. Nevertheless, Dr. Panigrahy relies upon the inhalation exposure in Hidajat to reach his conclusion about the oral exposure to VCDs. This is not scientifically reliable methodology.

Finally, the authors of Hidajat readily acknowledge that they were unable to control for certain confounding factors, including exposure to known carcinogens such as benzene and tobacco smoke, among others. (*Id.* at 483:23-484:5; 485:15-486:2). Similarly, Hidajat does not control for other lifestyle factors (*Id.* at 485:22-

486:2). Given that the study examined workers employed in the UK rubber industry in 1967, the inability to control for these critical factors represents a significant limitation of Hidajat. *See* Motion to Exclude Hecht, at Section II(B)(2)(stating that reliable toxicology methods must consider background risk).

Dr. Panigrahy makes the Hidajat study the centerpiece of his literature review. Given the numerous limitations of Hidajat, this reliance constitutes yet another crucial flaw in Dr. Panigrahy's methodology, and another reason why his testimony should be excluded pursuant to Rule 702.

E. Dr. Panigrahy's Opinion Regarding Cancer Development in "Downstream Organs" Lacks Any Scientific Basis to Conclude the Level of NDMA in Valsartan Can Escape the Liver.

Dr. Panigrahy opines that NDMA in VCDs causes liver, bladder, blood, gastric, intestinal, pancreatic, esophageal, prostate, lung, and kidney cancer in humans. (Panigrahy Rep. at 7). His premise is that NDMA travels first to the liver, and whatever is not metabolized there can escape and travel to other organs to inflict DNA damage and induce cancer development. (Panigrahy Dep. 440:2-9, 441:4-15). But his opinions with respect to the migration of NDMA (and cancer) to downstream organs other than the liver is not supported by any methodology, facts, or data, and therefore must be excluded as unreliable.

Dr. Panigrahy does not dispute that NDMA in VCDs is first metabolized in the liver by a process known as "first-pass" metabolism. (Panigrahy Dep. 438:14-

22). He also admits there is a level of NDMA that will be completely metabolized by the liver as part of first-pass metabolism. (*Id*. at 441:17-23). It follows, and Dr. Panigrahy agrees, that NDMA successfully metabolized by the liver in first-pass metabolism does not reach other downstream organs. (*Id*. at 440:24-441:4; 441:17-23). Stated another way, in order for NDMA to reach any other organ in the body, it would have to escape first-pass metabolism in the liver. (*Id*. at 445:9-19).

That is where Dr. Panigrahy's methodology again breaks down. Despite offering opinions that NDMA causes cancer in downstream organs, including bladder, blood, gastric, intestinal, pancreatic, esophageal, prostate, lung, and kidney cancer, Dr. Panigrahy cannot state, has no data, and has no opinion regarding what level of NDMA exposure would be necessary in order to escape metabolism in the liver and to expose other downstream organs or systems to NDMA. Moreover, he has no opinion whether the level of exposure to NDMA in the VCDs would escape the liver and expose other organs. He simply never considered it. His opinions regarding the development of cancer in those downstream organs has no foundation whatsoever and is wholly unreliable.

The Court should exclude Dr. Panigrahy's opinions with respect to cancer in non-liver organs and tissue systems for that reason. "In determining whether the expert is proposing to testify to scientific knowledge that will assist the trier of fact, the court must assess whether the methodology underlying the testimony is

scientifically valid and whether it can properly be applied to the facts in issue." *In re Diet Drugs*, 2001 WL 454586, at *7 (E.D. Pa. Feb. 1, 2001). "Furthermore, the court must examine the expert's conclusions in order to determine ***whether they can reliably follow from the facts*** known to the expert and the methodology used." *Id.* (emphasis added).

F. There is No Scientific Basis for Dr. Panigrahy's Opinion that NDEA Causes Cancer in Humans.

Dr. Panigrahy opines that both NDMA and NDEA can cause cancer in humans. Yet, with respect to NDEA, Dr. Panigrahy cites to no reliable human evidence, nor does he employ a reliable methodology, to support his opinion. Instead, Dr. Panigrahy simplistically relies on animal data regarding the mutagenicity of NDEA and then jumps to the conclusion that, because NDMA and NDEA are "similar" compounds, literature concerning the carcinogenicity of NDMA can be imputed to NDEA. (Panigrahy Dep. 504:6-20). This is not a scientifically valid approach, is not supported by evidence, and does not meet the stringent Rule 702 standard. *See* Motion to Exclude Hecht, at Section II(B)(5) (explaining disadvantages and problems with animal studies).

The fact of the matter is that there is a dearth of epidemiological evidence in the scientific literature to support the conclusion that NDEA at levels detected in Defendants' VCDs causes cancer in humans. Whereas there are a plethora of (limited and error-prone) dietary studies at least attempting to examine the

relationship between NDMA and cancer in humans, the same cannot be said about NDEA. Indeed, Dr. Panigrahy confirmed as much at his deposition, and, tellingly, he cites to just a single human study, Zheng, et al., to support his broad conclusion that NDEA in VCDs could cause any number of cancers. (*See* Panigrahy Dep. 506:20-22; Ex. F, Zheng, et al.). Notably, that lone study found a positive association between NDEA exposure and ***only one form of cancer***—pancreatic. Moreover, the exposures in that study were orders of magnitude higher than those at issue in affected VCDs. Plaintiffs' retained statistician, Dr. Madigan, admitted that the association in Zheng was based upon a lifetime cumulative exposure to 2,520,000 nanograms of NDEA. (Madigan Dep. 272:18-273:15, excerpts attached as Ex. G). Given that the tested levels of NDEA contained in the affected VCDs were relatively low, combined with the fact that none of the affected VCDs were on the market for more than six (6) years, the probability that any plaintiff in this litigation could have been exposed to 2,520,000 nanograms of NDEA from taking valsartan is at or near zero. (*See*, *e.g.*, Madigan Dep. 279:8-280:18, excerpts attached as Ex. G). By way of illustration, even if a hypothetical patient took Mylan's valsartan at the highest labeled dosage (320mg) with the highest level of NDEA detected in any active pharmaceutical ingredient ("API") batch ever produced (1.57ppm) for the entire six-year period Mylan's VCDs were on the market, the

patient's exposure to NDEA would be less than half of the exposure studied in Zheng.

A solitary study finding only a moderate association between levels of NDEA exceeding those at issue in this litigation and a single form of cancer does not provide a sound basis for Dr. Panigrahy's sweeping conclusion that NDEA in affected VCDs could lead to multiple different types cancer. Moreover, Dr. Panigrahy's reliance on NDMA studies to extrapolate a conclusion about NDEA—a separate and distinct chemical compound—is inherently flawed and unreliable. (Gibb Dep. 351:13-352:6, excerpts attached as Ex. H). Accordingly, Dr. Panigrahy should not be permitted to testify that NDEA in any of the affected VCDs can cause cancer in humans. Alternatively, if Dr. Panigrahy is permitted to offer such an opinion with respect to NDEA, it should be limited to pancreatic cancer because no study of human data supports an association between NDEA and any other form of cancer alleged by Plaintiffs in this litigation.

II. DR. PANIGRAHY RELIES ON UNRELIABLE DATA TO ASSESS EXPOSURE, RENDERING HIS OPINION UNRELIABLE.

Dr. Panigrahy's opinion rests on unreliable data that does not provide a reasonable assessment of the levels of NDEA or NDMA Plaintiffs may have experienced by ingesting finished dosage valsartan tablets. Specifically, Dr. Panigrahy failed to even calculate, let alone use, the average NDMA and NDEA levels contained in VCDs sold in the United States, despite the fact that this

information was readily available to him. Further, the data on which Dr. Panigrahy ultimately relied includes data for products that were never sold in the United States, further demonstrating the unreliability of his opinions. *See* Motion to Exclude Hecht, at Section I(A)(2), at p. 14 (explaining that unreliable underlying data make an opinion unreliable).

Exposure levels must be considered at the general causation stage, particularly where there exists a background rate for each of the cancers alleged by Plaintiffs, in order to assess if Plaintiffs' alleged cancers were actually caused by the drugs at issue. *See Hardeman v. Monsanto Co.*, 997 F.3d 941, 963 (9th Cir. 2021) ("To establish general causation, Hardeman's experts needed to show that glyphosate can cause NHL at exposure levels people realistically may have experienced."); *Soldo v. Sandoz Pharms. Corp.*, 244 F. Supp. 2d 434, 533 (W.D. Pa. 2003) (noting "[t]he need for statistically significant epidemiology is particularly acute" in a case where the disease occurs in the general population in order "to determine whether any given case of [the disease] could possibly be attributable to a particular drug"); *McMunn v. Babcock & Wilcox Power Generation Grp., Inc.*, 2013 WL 3487560, at *24 (W.D. Pa. July 12, 2013) (rejecting general causation expert opinion that "uranium is capable of inducing each and every type of cancer" in part because the expert "had no basis in the studies to infer that plaintiffs' risk from facility exposure was 'substantial' in comparison either to other established risk factors or to the

background incidence of cancer from unexplained causes"). Further, "when an expert opinion is based on data, a methodology, or studies that are simply inadequate to support the conclusions reached, *Daubert* and Rule 702 mandate the exclusion of that unreliable opinion testimony." *Amorgianos v. Nat'l R.R. Passenger Corp.*, 303 F.3d 256, 266 (2d Cir. 2002); *see also In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 749 n. 19 (3d Cir. 1994) ("[I]f the judge thinks that the expert would reach a different conclusion if he was not able to rely on this data, a conclusion that would no longer help the plaintiff (or defendant) to prove his or her case, the district court can exclude his opinion as irrelevant."). Because Dr. Panigrahy's opinions are based on unreliable data with respect to potential NDMA and/or NDEA exposure to Plaintiffs, they should be excluded under Rule 702.

A. Dr. Panigrahy Cherry-Picks The Highest Level Of NDMA And/Or NDEA In The Manufacturers' API Rather Than Consider The Average NDMA And/Or NDEA Levels Contained In The Valsartan Finished Dose Tablets Distributed In The United States.

Dr. Panigrahy fails to make a reasonable assessment of the levels of NDEA or NDMA Plaintiffs may have experienced by ingesting Defendants' finished dosage valsartan tablets. The FDA thoroughly investigated the Manufacturer Defendants' recalled finished dosage tablets, including testing numerous batches from each manufacturer, and published the average level of NDMA and NDEA in each Manufacturer Defendants' tablets sold in the United States. *See* U.S. Food and Drug Administration, *Laboratory Analysis of Valsartan Products*, available at

https://www.fda.gov/drugs/drug-safety-and-availability/laboratory-analysis-valsartan-products (last accessed Oct. 27, 2021) ("FDA Laboratory Analysis") ("The analyses reflect average levels of the impurities present in a single tablet based on the strength of the tested medicines within the lots tested, which are identified in the table.").

Despite citing in his report the results of this FDA investigation, Dr. Panigrahy does not rely on this evidence to assess the potential exposure levels Plaintiffs may have experienced through ingesting Defendants' valsartan tablets, and testified that he didn't have "access" to this ***publicly available*** information. (*See* Panigrahy Rep. at 9 (citing FDA Laboratory Analysis) (noting "FDA conducted an investigation into the presence of NDMA and NDEA in valsartan containing products which revealed NDMA contamination levels as high as 20.19 micrograms (20,190 nanograms) per tablet and NDEA contamination levels as high as 1.31 micrograms (1,310 nanograms) per tablet"); Panigrahy Dep. at 507:21-23 ("Q. Did you ever look at FDA's testing of Mylan's finished dose product? A. No, I don't have that."); *Id.* at 508:19-24 ("Q. Why did you ignore or not report on FDA's finished dose testing Mylan's product? A. I didn't have – I didn't have that data. And what I was – I could only report on the data that I had access to.")).

Instead, Dr. Panigrahy notes that "[t]here were various levels of contamination reported across the different manufacturers" and cites to different

company documents containing test results. (Panigrahy Rep. at 10) (including, for example, "ZHP reported NDMA in the approximate range of 3.4 to 188.1 ppm for one process and ranging from ND to 73.9 for another process (ZHP00079920-9940)."). Notably, Dr. Panigrahy cites these results without mention of whether the API or finished dose products were tested by the manufacturer. (*Id.* at 10-11). This distinction is important given that Plaintiffs would never have ingested pure API but instead only ingested the finished dosage form tablets.[5]

Nevertheless, without distinction, Dr. Panigrahy compares the "levels" in the manufacturers' API to the FDA's acceptable intake limit by cherry-picking the respective highest NDMA and NDEA test result. (*Id*. at 10-11) ("For example, the batch containing 188.1 ppm of NDMA is 627 times higher than the acceptable intake established by the FDA. The batch containing 16.93 ppm of NDEA is 204 times higher than the acceptable intake established by the FDA."). This is an unacceptable use of inapplicable data.

B. Dr. Panigrahy Failed To Calculate Any Mean NDMA Or NDEA Exposure Levels That Plaintiffs May Have Actually Experienced,

[5]And Dr. Panigrahy is unquestionably aware of this distinction between API and finished dosage tablets because, in certain instances, he estimates how many nanograms of NDEA or NDMA would be in a 320 mg valsartan tablet based on an API testing result. *See, e.g.*, Panigrahy Rep. at 9-10 ("For example, Zhejiang Huahai Pharmaceutical (ZHP) batches of valsartan have been recorded to contain 188.1 ppm of NDMA (See ZHP 118/SOLCO00028261) which equates to 60,192 nanograms in a 320 mg tablet.").

And Instead Used Data Irrelevant To This Case To Inflate His Calculations.

In addition to the fact that Dr. Panigrahy relies on the levels of NDMA and/or NDEA in valsartan API rather than valsartan finished dose products, his opinions are unreliable because he did not even calculate, let alone rely on, any mean NDMA or NDEA exposure levels from that data. (*See* Panigrahy Dep. at 506:8-13 ("Q. [I]n connection with your work in this case, have you received information about NDEA levels in Mylan's commercialized API, did you make any attempt to calculate a mean concentration? A. So – no, . . ."); *Id.* at 510:23-511:17 ("Q: And if you wanted to consider all the facts, one of the things that you can – and if you wanted to determine whether or not the dose and duration from Mylan's valsartan-containing medications can cause cancer, **one of the things you could do is to calculate the mean exposure from test data that's available, right**? . . . **A. Correct.**" (emphasis added))).

Instead, Dr. Panigrahy relies on an internal ZHP document in which he alleges ZHP has "represented" or "reported" "the average ppm in the ZHP valsartan API made with the Zinc Chloride process." Panigrahy Rep. at 9-10, 88, 90. However, the internal ZHP document that Dr. Panigrahy relies upon for his "average" NDMA (not NDEA) level does not accurately reflect the exposure levels Plaintiffs may have experienced for two key reasons.

First, no Plaintiff took only ZHP's valsartan for the entirety of the time it was on the market; as Dr. Panigrahy testified, Plaintiffs "went to the pharmacy" and received "different valsartan batches, so there was not only Mylan [product], they may have gone to the pharmacy and gotten another valsartan tablet from a different" manufacturer. (Pangrahy Dep. at 502:7-13).

Second, for his calculations of the levels of NDMA in ZHP's valsartan API, Dr. Panigrahy relies on data related to valsartan API ***that was never used in products sold in the United States*** in order to distort the levels of NDMA in products that the Plaintiffs could have possibly ingested. Importantly, ***only USDMF grade valsartan API can be used for products sold in the United States***. However, the summary table relied upon by Dr. Panigrahy groups API test results by their product code and the workshop at ZHP in which those batches were manufactured, and includes non-USDMF grades of API, none of which could be used for products sold in the United States. (*See* Panigrahy Rep. at 88-90; Ex. I, Prinston 75838).

Table 3-11. Summary of NDMA test results of Valsartan

车间名称 Workshop	产品代号 Product Code	工艺 Process	标准 Spec.	检测批次 Batches	结果范围 ppm Range (ppm)	平均值 ppm Avg.(ppm)
W02 车间 Workshop W02	D5191	氯化锌 $ZnCl_2$	EDMF/USDMF	1568	0.3-240.1	65.1
W02 车间 Workshop W02	D5195	三乙胺 TEA	EDMF/USDMF	64	0-7.7	0.9
2 车间 Workshop 2	C5354	三乙胺 TEA	EDMF/USDMF	122	0-37.3	1.8
2 车间 Workshop 2	C5355	氯化锌 $ZnCl_2$	EDMF/USDMF	1579	0.4-136.3	63.4
2 车间 Workshop 2	C5356	三乙胺/氯化锌 TEA/ $ZnCl_2$	CP	195	8.7-138.9	65.8
4 车间 Workshop 4	C5069	三乙胺 TEA	EDMF/USDMF	338	0-73.9	5.5
12/13 车间 Workshop 12/13	C5271	氯化锌 $ZnCl_2$	USP	987	0-166.7	70.8
13 车间 Workshop 13	C5523	氯化锌 $ZnCl_2$	CEP/USDMF	2157	0-188.1	56.7

Ex. I.

As illustrated above, the table relied upon by Dr. Panigrahy includes a column for "Spec.", which indicates the different grades of API that were manufactured in that particular workshop. *See* Ex. I (noting, in the first row, that 1568 batches were tested that were manufactured in Workshop W02, including some batches manufactured according to EDMF (Europe) specifications and some according to USDMF (U.S.) specifications). However, Dr. Panigrahy relied on three rows of data from this table (highlighted) that indicates the batches tested in those groups ***included non-USDMF grade API*** (*i.e.*, EDMF and CEP grade API). Because only

USDMF grade valsartan API (and *not* EDMF or CEP grade API) can be used in finished dose products sold in the United States, the results of the testing summarized in this table include batches of API that ***could not have been ingested by a potential plaintiff in this litigation***—making the "average" NDMA amount an unreliable source for potential NDMA exposure levels from ZHP products.[6]

In sum, despite claiming at his deposition that he "did a range" for levels of NDMA in Defendants' products to which Plaintiffs may have been exposed (Panigrahy Dep. at 498:11-17), Dr. Panigrahy relies on only the highest NDMA and/or NDEA level reported in company documents, as well as one company document summarizing data on API that included API not used in the finished dose products ingested by Plaintiffs in this case. *Paoli*, 35 F.3d at 749 ("[W]hen a trial judge analyzes whether an expert's data is of a type reasonably relied on by experts in the field, he or she should assess whether there are good grounds to rely on this

[6] Defendants do not concede that it would be reliable to calculate the mean NDMA/NDEA exposure that Plaintiffs may have plausibly experienced through ingesting Defendants' finished dose tablets by using API testing data. *See* supra at Section II. A. However, Plaintiffs had in their possession all of the information they needed to assess the mean NDMA/NDEA levels in ZHP's valsartan API—and still chose not to do so. Specifically, upon Plaintiffs' insistence, ZHP produced in August 2020 all nitrosamine testing data for USDMF-grade valsartan API batches. *See* 6-25-21 Hrg. Tr. [Dkt. 1356] at 42:10-22 (Counsel for ZHP: "[W]hat [Plaintiffs] have and what [ZHP] ha[s] produced are all of the testing results for USDMF-grade valsartan API . . . ."). Presumably, Plaintiffs chose not to share this information with Dr. Panigrahy in order to artificially inflate the NDMA levels upon which he based his conclusions.

data to draw the conclusion reached by the expert."). Dr. Panigrahy employs this unreliable method by failing to calculate a mean exposure even though he expressly admitted at his deposition that the manufacturers' tablets contained different amounts of NDMA and NDEA and Plaintiffs would have received a mix of these tablets. *Id.* at 742 ("*Daubert* holds that an inquiry into the reliability of scientific evidence under Rule 702 requires a determination as to its scientific validity."). Further, because Dr. Panigrahy's assessment of exposure is not based in science, his opinions do not fit the facts of the case and will not assist the jury. *In re Diet Drugs Prod. Liab. Litig.*, 706 F. 3d 217, n.7 (3d Cir. 2013) ("To determine whether [an opinion] is helpful, this Court looks to the 'proffered connection between the scientific research or test result to be presented and particular disputed factual issues in the case.'").

Accordingly, Dr. Panigrahy's opinions should be excluded because he provides no basis to establish that Plaintiffs are at an increased risk of any cancer based on the NDMA or NDEA exposure they may have reasonably experienced from Defendants' products above the baseline background risk of developing the different types of cancers alleged by Plaintiffs.

III. DR. PANIGRAHY IS NOT QUALIFIED TO OPINE REGARDING WHETHER NDMA OR NDEA CAN CAUSE HUMAN CANCER.

Finally, the Court should exclude Dr. Panigrahy's opinions in their entirety because he is not qualified to opine as to whether the NDMA or NDEA in VCDs can

cause human cancer. To render expert opinions, a witness must be sufficiently qualified as an expert "by knowledge, skill, experience, training, or education." Fed. R. Evid. 702; *see also* Motion to Exclude Hecht, at section I(A)(1) (explaining qualifications requirement for expert testimony). Gaining knowledge on a subject solely for the purposes of litigation, rather than as the result of the witness's general academic research, does not qualify the witness as an expert in the litigation-driven subject matter. *See, e.g.*, *Soldo v. Sandoz Pharms. Corp.*, 244 F. Supp. 2d 434, 527 (E.D. Pa. 2003) (noting that expert opinions generated as the result of litigation have less credibility than opinions generated as the result of academic research or other forms of "pure" research).

Although an expert may be "generally qualified" he may nonetheless be properly excluded if he "lack[s] qualifications to testify outside his area of expertise." *Calhoun v. Yamaha Motor Corp., U.S.A.*, 350 F.3d 316, 322 (3d Cir. 2003) (affirming prohibition of expert qualified in psychology and human factors from offering opinions regarding the necessity of warnings restricting operation of jet skis to those older than a certain age, even though the expert was otherwise qualified to testify about proper warnings in general). *See also U.S. v. Faines*, 216 Fed. App'x 227, 230 (3d Cir. 2007) (affirming preclusion of a research scientist from performing a latent fingerprint comparison during her testimony because it was outside her area of expertise); *Barrett v. Atlantic Richfield Co.*, 95 F.3d 375, 382 (5th

Cir. 1996) (holding that ecologist with expertise in behavior patterns of rats was not qualified to opine on source of chromosomal damage exhibited by rats or whether humans faced increased health risks from exposure to chemicals).

As noted, Plaintiffs' causation theory, expressed through Dr. Panigrahy, is that any genotoxic compound capable of causing DNA mutations and shown to be carcinogenic in animals is necessarily carcinogenic in humans, regardless of dose and without regard to the inherent human defenses to carcinogenicity, including metabolic and DNA repair capacities. Those opinions have no logical connection to Dr. Panigrahy's credentials. Dr. Panigrahy's research background related to cancer treatment is not related to the general causation inquiry at issue, i.e., cancer development. Moreover, although Dr. Panigrahy holds a medical degree from Boston University, he has no advanced degree or training in cancer biology. (Panigrahy Dep. at Ex. 2). He is not licensed to practice medicine, is not board-certified in any specialty, and is not board-eligible. (Panigrahy Rep. at 1; Panigrahy Dep. at 80:13-22). Dr. Panigrahy did not complete his residency program. (Panigrahy Dep. 73:13-23). As such, his medical education did not include an oncology rotation. (*Id.* at 70:2-71:1).

Not only does Dr. Panigrahy have no experience with NDMA or NDEA—the specific compounds at issue here—he has never studied genotoxic compounds of any kind up until Plaintiffs retained him in this litigation. (*Id.* at 216:23-217:16). He

has never published any research about genotoxic compounds. (*Id*. at 216:17-21). He has never studied the effects of NDMA. (*Id*. at 121:6-13). He does not study DNA adducts. (*Id*. at 275:15-18). He does not study DNA repair, the mechanism by which human cells remove DNA adducts prior to cell replication and thereby avoid the formation of a DNA mutation. (*Id*. at 253:25-254:2; Chodosh Dep. at 489:3-25). He is not a toxicologist, although he offers toxicology opinions. (Panigrahy Dep. 119:4-6). Likewise, Dr. Panigrahy is not a pathologist, pharmacologist, pharmacokinetics expert, or statistician. (*Id.* at 82:1-5, 121:15-23, 122:22–126:7, 126:25–127:10).

Dr. Panigrahy describes his own expertise as pertaining to *non*-genotoxic mechanisms, not genotoxic compounds. (*Id.* at 218:9-12) ("So our expertise, I would agree, is more nongenotoxic mechanisms, such as inflammation, angiogenesis as a lab."). His research centers on studying particular mechanisms of extant cancers, not cancer causation or whether specific genotoxic compounds can cause cancer. (*Id.* 216:23-217:16). According to Dr. Panigrahy, his lab has "world-leading expertise in helping pioneer the field of inflammation resolution in cancer." (Panigrahy Rep. at 3). That expertise has no relation to cancer causation, genotoxic compounds or the nitrosamines at issue here, and it does not qualify Dr. Panigrahy to opine on whether NDMA or NDEA cause cancer in humans.

"Specialized knowledge alone . . . is not sufficient to satisfy Rule 702. The Rule also requires the witness to have specialized knowledge *relating to the area of testimony*. In other words, specialized knowledge must be relevant to the area of inquiry." *Fedor v. Freightliner, Inc.*, 193 F. Supp. 2d 820, 828 (E.D. Pa. April 4, 2002) (emphasis added); *see also In re: Tylenol (Acetaminophen) Mktg., Sales Pracs., & Prod. Liab. Litig.*, 2016 WL 4538621, at *4 (E.D. Pa. Aug. 31, 2016); *In re Diet Drugs (Phentermine, Fenfluramine, Dexfenfluramine) Prod. Liab. Litig.*, 2000 WL 876900, at *6 (E.D. Pa. June 20, 2000) (citations omitted) ("A court should exclude proffered expert testimony if the subject of the testimony lies outside the witness's area of expertise. . . . In other words, a party cannot qualify an expert generally by showing that the expert has specialized knowledge or training that would qualify him or her to opine on some other issue."). Dr. Panigrahy's opinions regarding a purported causal link between exposure to NDMA and NDEA and the development of cancer—let alone cancer in humans at the doses and durations of exposure at issue in this litigation—admittedly fall outside his area of expertise. As an example of his lack of expertise, Dr. Panigrahy made no effort to evaluate the specific levels determined in the finished dose testing of VCDs here. He concedes that risk calculations such as linear back extrapolation or benchmark dose calculations are the way scientists differentiate between safe versus potentially carcinogenic levels of exposure to a suspected mutagenic compound like NDMA.

(Panigrahy Dep. 45:6-11). However, prior to his involvement in this litigation he had never performed a TD 50 linear back extrapolation[7] for any potential carcinogen. (*Id.* at 129:23-130:2). He has never performed a benchmark dose level calculation for any potential carcinogen. (*Id.* at 130:3-7). And he has never done a risk assessment that evaluated whether exposure to any level of a potential carcinogen was likely to cause cancer in humans. (*Id.* at 130:8-13). Instead, as discussed below, Dr. Panigrahy assumes, contrary to accepted science and basic logic, that ***any*** exposure to a potential mutagen can be carcinogenic. (Panigrahy Rep. at 83). These opinions, too, should be excluded based on his lack of qualifications to offer them.

CONCLUSION

Based on the above-cited authority, Defendants respectfully request that the Court exclude Dr. Panigrahy's opinions. Dr. Panigrahy is not qualified to render an opinion as to whether exposure to NDMA or NDEA in VCDs can cause human cancer. Moreover, he does not address the question before the Court at the general causation stage: whether the NDMA level to which valsartan patients could reasonably have been exposed increases the risk of cancer. Dr. Panigrahy employs

[7]The TD50 linear back extrapolation is a calculation using rodent data of the 50% toxic dose level, i.e. the "TD50", then calculating a 1 in 100,000 incidence of cancer. The TD50 approach does not consider any human data such as DNA repair. *See* ANDREW TEASDALE, GENOTOXIC IMPURITIES: STRATEGIES FOR IDENTIFICATION AND CONTROL 125 (2010).

flawed methodology and flawed data in reaching his conclusions, which renders his opinions unhelpful, unreliable and inadmissible under Rule 702 and *Daubert*. For these reasons as set forth above, the Court should exclude or, in the alternative, limit Dr. Panigrahy's opinions.

Dated: November 1, 2021

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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on November 1, 2021, I electronically filed the foregoing with the Clerk of the Court by using the CM/ECF system which will send a notice of electronic filing to all CM/ECF participants in this matter.

/s/ Seth A. Goldberg
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